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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,702	12/20/2005	David Hone	4115-178	4972

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INTELLECTUAL PROPERTY / TECHNOLOGY LAW
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EXAMINER	
KINSEY WHITE, NICOLE ERIN	
ART UNIT	**PAPER NUMBER**
1648	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/525,702	**Applicant(s)** HONE, DAVID	
	Examiner Nicole Kinsey White, PhD	**Art Unit** 1648	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 13 November 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on ___. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: ___. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): ___.
6. ☐ Newly proposed or amended claim(s) ___would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: ___.
   Claim(s) objected to: ___.
   Claim(s) rejected: *1-16, 19-30,40-42,62,63 and 79*.
   Claim(s) withdrawn from consideration: *17 and 18*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: ___.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: ___.

DETAILED ACTION

Election/Restrictions

The restriction mailed February 9, 2007 required applicant to elect either foreign or endogenous immunogens. Applicant was further required to elect a sub-species as follows:

If applicants elect foreign immunogens, applicants must also elect one of (a)-(e) of claim 13 as follows: (a) viral proteins, (b) bacterial proteins, (c) parasite proteins, (d) cytokines, chemokines, and immunoregulatory agents, and (e) therapeutic agents.

If applicants elect endogenous immunogens, applicants must also elect one of (a)-(e) of claim 17 as follows: (a) cellular proteins, (b) immunoregulatory agents, (c) therapeutic agents, (d) tumor immunogens, and (e) autoimmune immunogens.

The obvious typographical error (i.e., reciting foreign instead of endogenous) in the preceding paragraph has been corrected.

Applicants elected foreign immunogens and subspecies (a) viral proteins from claim 13. Therefore, applicant's additional election of cellular proteins from claim 17 will not be considered at this time as the election is directed to a non-elected species.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 40-42 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is maintained. The claims contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)).

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

Nature of the invention. The claims are drawn to a method of vaccination comprising administering the claimed rdsRP to a subject. Thus, the claims encompass the prevention of diseases by administering a vaccine.

State of the Art. The instant invention is drawn to a method of vaccination comprising administering a rdsRP to a subject. The term "vaccine", by definition, implies a preparation intended for active immunological prophylaxis; e.g., preparations of killed microbes of virulent strains or living microbes of attenuated (variant or mutant) strains; or microbial, fungal, plant, protozoa, or metazoan derivatives or products. Prophylaxis is defined as the prevention of disease or of a process that can lead to disease. Although nearly any protein when inoculated can cause an immune reaction,

the prophylactic nature of this reaction is not guaranteed and has to be experimentally determined.

Guidance in the Specification. The claimed invention is directed to a method for vaccination by administering to a subject a rdsRP. The method is not strictly limited to *in vitro* treatments and encompasses treating human subjects *in vivo*. There is insufficient disclosure to reasonably predict that the methods and compositions of the instant specification would prevent a disease after vaccination. Applicants have only described methods for making the rdsRP and provide prophetic examples (see Examples 8-11) describing the *in vitro* infection of dendritic cells and the *in vivo* vaccination of mice. There is no guidance or description for vaccinating subjects or showing an art recognized correlation between any *in vitro* data and the scope of the claimed invention. Thus, one is left with speculation and an invitation to experiment.

Working Examples. There are only prophetic examples (see Examples 8-11) describing the *in vitro* infection of dendritic cells and the *in vivo* vaccination of mice. There is no working example disclosed in the specification demonstrating the vaccination of a subject with rdsRP and prevention of a disease following vaccination.

In view of the lack of guidance, objective evidence, and predictability in the specification, it would require undue experimentation by one of ordinary skill in the art to practice the claimed invention.

The instant invention, based on the evidence as a whole, in light of the factors articulated by the court in *In re Wands*, lacks an enabling disclosure.

Response to Arguments

Applicants argue that one of skill in the art would have been enabled to perform the clamed method of vaccination.

It appears applicants are arguing whether or not one of ordinary skill in the art can perform the recited method steps (i.e., administering the claimed rdsRP to a subject) based on the teachings of the specification.

This enablement rejection does not relate to performing the steps to vaccinate a subject, but instead relates to the outcome (i.e., vaccination). As stated above, the claims are drawn to a method of vaccination comprising administering the claimed rdsRP to a subject. Thus, the claims encompass the prevention of diseases by administering a vaccine. The term "vaccine", by definition, implies a preparation intended for active immunological prophylaxis; e.g., preparations of killed microbes of virulent strains or living microbes of attenuated (variant or mutant) strains; or microbial, fungal, plant, protozoa, or metazoan derivatives or products. Prophylaxis is defined as the prevention of disease or of a process that can lead to disease. Although nearly any protein when inoculated can cause an immune reaction, the prophylactic nature of this reaction is not guaranteed and has to be experimentally determined.

For example, the claimed method encompasses administering a rdsRP with an HIV gene as the passenger gene. However, it is well known in the art and even to the general public that medical science, despite decades of intense research, has not found any antigen, immunogen, or compound that can be credibly used as a vaccine against HIV.

The difficulties inherent to developing an HIV vaccine are well known. For the sake, of clarity, some of those problems are outlined here:

1) the extensive genomic diversity associated with HIV, due in large part to error prone reverse transcription of its RNA genome,

2) the fact that the modes of viral transmission include virus-infected mononuclear cells, which pass the infecting virus to other cells in a covert form (cell to cell transmission), as well as via free virus transmission,

3) the existence of latent forms of the virus,

4) the complexity and variation of the elaboration of the disease, and

5) the property of some portions of HIV proteins or peptides to actually cause immunosuppression or other detrimental consequences.

The existence of these obstacles prevents one of ordinary skill in the art from accepting any therapeutic regimen on its face given the intense interest in developing HIV treatments or vaccines and the lack of success in doing so.

As discussed above, applicants are claiming a method of vaccination via a vaccine, which by definition, implies a preparation intended for active immunological prophylaxis against an antigen(s). Applicants have not shown that the "vaccine" provides a vaccinated subject any protection against any antigen. Furthermore, applicants have not shown *in vitro* infection of cells or *in vitro* activation of immune cells against the expressed antigen or a correlation between the *in vitro* data and *in vivo* protection. Applicants have not provided any examples or any guidance for making and using a vaccine that provides immunological prophylaxis against any antigen.

Applicants' prophetic examples do not provide guidance with regard to whether or not the antigen in the context of a dsRNA is properly expressed in a host, is properly presented on antigen presenting cells, activates immune cells, causes the production of antibodies or cytotoxic T cell responses to the expressed antigen, or produces a sufficient immune response to provide protection. Therefore, one of ordinary skill in the art could not predict whether or not the claimed invention would be a vaccine.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-30, 62-63 and 79 remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-19 of U.S.

Patent No. 7,018,835 ("the '835 patent"). Although the conflicting claims are not identical, they are not patentably distinct from each other because there is overlapping subject matter between the groups of claims. Specifically, the scope of the '835 claims encompasses the scope of the instant claims. **NOTE: This rejection is being maintained until the Terminal Disclaimer filed on November 13, 2007 has been approved.**

The patented claims are drawn to a double stranded RNA (dsRNA) phage that expresses at least one genetic sequence in eukaryote cells, comprising: a cap independent translation enhancer (CITE); and at least one genetic sequence that is expressed in a eukaryote cell, wherein said CITE and said at least one genetic sequence are functionally linked and are incorporated into one or more dsRNA segments in the dsRNA. The dsRNA phage can further comprise antigens, a bioactive protein, an immunoregulatory protein, an antisense RNA, a catalytic RNA or an immunogen.

The instant claims are directed to a recombinant double stranded RNA phage (rdsRP) encoding a double stranded RNA eukaryotic expression cassette for expression in eukaryotic cells, the rdsRP comprising: at least one segment of a double stranded RNA phage (dsRP) and an internal ribosome entry site (IRES) nucleotide sequence incorporated into the at least one segment of the dsRP. The specification states that CITE and IRES are the same (see page 5, lines 19-22). The rdsRP can further comprise an adjuvant (i.e., a bioactive protein).

With regard to amplifying the rdsRP in a bacterial host as recited in the instant claims, it would have been obvious to amplify the rdsRP of the '835 patent in a bacterial host because that is the most common method used to amplify phages.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nicole Kinsey White, PhD whose telephone number is (571) 272-9943. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Nicole Kinsey White, PhD
Examiner
Art Unit 1648

/nkw/

/Stacy B. Chen/ 1-16-2008
Primary Examiner, TC1600